

AMENDMENTS TO THE CLAIMS

Please cancel Claims 10, 11, 18 and 20-27, without prejudice, as shown below.

Please amend Claims 1, 6, 29 and 37 as shown in the following list of claims.

1. (Currently Amended) An ApoA-I agonist compound comprising:

(i) a 22 to 29-residue D-enantiomeric peptide or peptide analogue which forms an amphipathic α -helix in the presence of lipids and which comprises formula (I):

$Z_1-X_1-X_2-X_3-X_4-X_5-X_6-X_7-X_8-X_9-X_{10}-X_{11}-X_{12}-X_{13}-X_{14}-X_{15}-X_{16}-X_{17}-X_{18}-X_{19}-X_{20}-X_{21}-X_{22}-X_{23}-Z_2$

or a pharmaceutically acceptable salt thereof, wherein:

X_1 is D-Ala (a), Gly (G), D-Gln (q), D-Asn (n), D-Asp (d) or D-Pro (p);

X_2 is a D-enantiomeric aliphatic residue;

X_3 is D-Leu (l) or D-Phe (f);

X_4 is a D-enantiomeric acidic residue;

X_5 is D-Leu (l) or D-Phe (f);

X_6 is D-Leu (l) or D-Phe (f);

X_7 is a D-enantiomeric hydrophilic residue;

X_8 is a D-enantiomeric acidic or a basic residue;

X_9 is D-Leu (l) or Gly (G);

X_{10} is D-Leu (l), D-Trp (w) or Gly (G);

X_{11} is a D-enantiomeric hydrophilic residue;

X_{12} is a D-enantiomeric hydrophilic residue;

X_{13} is Gly (G) or a D-enantiomeric aliphatic residue;

X_{14} is D-Leu (l), D-Trp (w), Gly (G) or D-Nal;

X_{15} is a D-enantiomeric hydrophilic residue;

X_{16} is a D-enantiomeric hydrophobic residue;

X_{17} is a D-enantiomeric hydrophobic residue;

X_{18} is D-Gln (q), D-Asn (n) or a D-enantiomeric basic residue;

X_{19} is D-Gln (q), D-Asn (n) or a D-enantiomeric basic residue;

X_{20} is a D-enantiomeric basic residue;

X_{21} is a D-enantiomeric aliphatic residue;

X_{22} is a D-enantiomeric basic residue;

X_{23} is absent or a D-enantiomeric basic residue;

Z_1 is R_2N- or $RC(O)NR-$;

Z_2 is $-C(O)NRR$, $-C(O)OR$ or $-C(O)OH$ or a salt thereof;

each R is independently -H, (C₁-C₆) alkyl, (C₁-C₆) alkenyl, (C₁-C₆) alkynyl, (C₅-C₂₀) aryl, (C₆-C₂₆) alkaryl, 5-20 membered heteroaryl, 6-26 membered alkheteroaryl or a 1 to 7-residue peptide or peptide analogue in which one or more bonds between residues 1 through 7 are independently a substituted amide, an isostere of an amide or an amide mimetic; and

each “ - ” between residues X₁ through X₂₃ independently designates an amide linkage, a substituted amide linkage, an isostere of an amide or an amide mimetic; or

~~(ii) a 14 to 28-residue deleted D-enantiomeric peptide or peptide analogue according to formula (I) in which at least one and up to eight of residues X₁, X₂, X₃, X₄, X₅, X₆, X₇, X₈, X₉, X₁₀, X₁₁, X₁₂, X₁₃, X₁₄, X₁₅, X₁₆, X₁₇, X₁₈, X₁₉, X₂₀, X₂₁ and X₂₂ are optionally deleted; or~~

(ii) ~~(iii)~~ a 22 to 29-residue altered D-enantiomeric peptide or peptide analogue according to formula (I) in which at least one of residues X₁, X₂, X₃, X₄, X₅, X₆, X₇, X₈, X₉, X₁₀, X₁₁, X₁₂, X₁₃, X₁₄, X₁₅, X₁₆, X₁₇, X₁₈, X₁₉, X₂₀, X₂₁, X₂₂ or X₂₃ is conservatively substituted with another D-enantiomeric residue.

2. (Canceled).

3. (Previously Presented) The ApoA-I agonist compound of Claim 1 which is the altered D-enantiomeric peptide or peptide analogue according to formula (I).

4. (Previously Presented) The ApoA-I agonist compound of Claim 3 in which the D-enantiomeric hydrophobic residues are fixed according to formula (I) and at least one non-fixed residue is conservatively substituted with another D-enantiomeric residue.

5. (Previously Presented) The ApoA-I agonist compound of Claim 4 in which:

X₁ is D-Pro (p), Gly (G) or D-Ala (a);

X₂ is D-Ala (a), D-Leu (l) or D-Val (v);

X₃ is D-Leu (l) or D-Phe (f);

X₅ is D-Leu (l) or D-Phe (f);

X₆ is D-Leu (l) or D-Phe (f);

X₉ is D-Leu (l) or Gly (G);

X₁₀ is D-Leu (l), D-Trp (w) or Gly (G);

X₁₃ is D-Leu (l), Gly (G) or D-Aib;

X₁₄ is D-Leu (l), D-Nal, D-Trp (w) or Gly (G);

X₁₆ is D-Ala (a), D-Nal, D-Trp (w), Gly (G), D-Leu (l) or D-Phe (f);

X₁₇ is D-Leu (l), Gly (G) or D-Nal;

X₂₁ is D-Leu (l); and

at least one of X₄, X₇, X₈, X₁₁, X₁₂, X₁₅, X₁₈, X₁₉, X₂₀, X₂₂ and X₂₃ is conservatively substituted with another D-enantiomeric residue.

6. (Currently Amended) The ApoA-I agonist compound of Claim 3 5 in which the D-enantiomeric hydrophilic residues are fixed according to formula (I) and at least one non-fixed residue is conservatively substituted with another D-enantiomeric residue.

7. (Previously Presented) The ApoA-I agonist compound of Claim 6 in which:

X₄ is D-Asp (d) or D- Glu (e);

X₇ is D-Lys (k), D-Arg (r) or D-Orn;

X₈ is D-Asp (d) or D-Glu (e);

X₁₁ is D-Asn (n) or D-Gln (q);

X₁₂ is D-Glu (e) or D-Asp (d);

X₁₅ is D-Asp (d) or D-Glu (e);

X₁₈ is D-Gln (q), D-Asn (n), D-Lys (k) or D-Orn;

X₁₉ is D-Gln (q), D-Asn (n), D-Lys (k) or D-Orn;

X₂₀ is D-Lys (k) or D-Orn;

X₂₂ is D-Lys (k) or D-Orn;

X₂₃ is absent or D-Lys (k); and

at least one of X₁, X₂, X₃, X₅, X₆, X₉, X₁₀, X₁₃, X₁₄, X₁₆, X₁₇ and X₂₁ is conservatively substituted with another D-enantiomeric residue.

8. (Previously Presented) The ApoA-I agonist compound of Claim 7 in which X₃ is D-Leu (l) or D-Phe (f), X₆ is D-Phe (f), X₉ is D-Leu (l) or Gly (G), X₁₀ is D-Leu (l) or D-Trp (w) or Gly (G) and at least one of X₁, X₂, X₅, X₁₃, X₁₄, X₁₆, X₁₇ and X₂₁ is conservatively substituted with another D-enantiomeric residue.

9. (Previously Presented) The ApoA-I agonist compound of Claim 4 or 6 in which the substituting D-enantiomeric residue is classified within the same sub-category as the substituted D-enantiomeric residue.

10.-11. (Canceled).

12. (Previously Presented) The ApoA-I agonist compound of Claim 1 which is a 22-23 residue D-enantiomeric peptide or peptide analogue according to formula (I).

13. (Previously Presented) The ApoA-I agonist compound of Claim 12 in which:

the “-” between residues designates -C(O)NH-;

Z₁ is H₂N-; and

Z₂ is -C(O)OH or a salt thereof.

14. (Previously Presented) The ApoA-I agonist compound of Claim 13, in which:

X₁ is D-Ala (a), Gly (G), D-Asn (n), D-Gln (q), D-Asp (d) or D-Pro (p);

X₂ is D-Ala (a), D-Val (v) or D-Leu (l);

X₃ is D-Leu (l) or D-Phe (f);

X₄ is D-Asp (d) or D-Glu (e);

X₅ is D-Leu (l) or D-Phe (f);

X₆ is D-Leu (l) or D-Phe (f);

X₇ is D-Lys (k), D-Arg (r) or D-Orn;

X₈ is D-Asp (d) or D-Glu (e);

X₉ is D-Leu (l) or Gly (G);

X₁₀ is D-Leu (l), D-Trp (w) or Gly (G);

X₁₁ is D-Asn (n) or D-Gln (q);

X₁₂ is D-Glu (e) or D-Asp (d);

X₁₃ is Gly (G), D-Leu (l) or D-Aib;

X₁₄ is D-Leu (l), D-Nal, D-Trp (w) or Gly (G);

X₁₅ is D-Asp (d) or D-Glu (e);

X₁₆ is D-Ala (a), D-Nal, D-Trp (w), D-Leu (l), D-Phe (f) or Gly (G);

X₁₇ is Gly (G), D-Leu (l) or D-Nal;

X₁₈ is D-Gln (q), D-Asn (n), D-Lys (k) or D-Orn;

X₁₉ is D-Gln (q), D-Asn (n), D-Lys (k) or D-Orn;

X₂₀ is D-Lys (k) or D-Orn;

X₂₁ is D-Leu (l);

X₂₂ is D-Lys (k) or D-Orn; and

X₂₃ is absent or D-Lys (k).

15. (Previously Presented) The ApoA-I agonist compound of Claim 14, in which X₂₃ is absent.

16. (Previously Presented) The ApoA-I agonist compound of Claim 13 or 14, in which one of X₁₈ or X₁₉ is D-Gln (q) or D-Asn (n) and the other of X₁₈ or X₁₉ is D-Lys (k) or D-Orn.

17. (Withdrawn) The ApoA-I agonist compound of Claim 14 in which each of X₉, X₁₀, X₁₃, X₁₄, X₁₅ and X₁₇ is other than Gly (G).

18. (Withdrawn) The ApoA-I agonist compound of Claim 14 in which one of X₉, X₁₀, X₁₃, X₁₄, X₁₅ and X₁₇ is Gly (G) and the others are other than Gly (G).

19.-28. (Canceled).

29. (Currently Amended) An ApoA-I agonist-lipid complex comprising an ApoA-I agonist compound and a lipid, wherein the ApoA-I agonist compound is a peptide or peptide analogue according to Claim 1, ~~a multimeric ApoA-I agonist compound according to Claim 20, a multimeric ApoA-I agonist compound according to Claim 21, or a multimeric ApoA-I agonist compound according to Claim 22.~~

30.-33. (Canceled).

34. (Previously Presented) The ApoA-I agonist-lipid complex of Claim 29 in which the lipid is sphingomyelin.

35. (Previously Presented) The ApoA-I agonist-lipid complex of Claim 34 which is in the form of a lyophilized powder.

36. (Canceled).

37. (Currently Amended) A pharmaceutical composition comprising an ApoA-I agonist compound and a pharmaceutically acceptable carrier, excipient or diluent, wherein the ApoA-I agonist compound is a peptide or peptide analogue according to Claim 1, ~~a multimeric~~

~~ApoA-I agonist compound according to Claim 20, a multimeric ApoA-I agonist compound according to Claim 21, or a multimeric ApoA-I agonist compound according to Claim 22.~~

38.-41. (Canceled).

42. (Previously Presented) The pharmaceutical composition of Claim 37, in which the ApoA-I agonist is in the form of an ApoA-I agonist-lipid complex, said complex comprising the ApoA-I agonist compound and a lipid.

43. (Canceled).

44. (Withdrawn) A method of treating a subject suffering from a disorder associated with dyslipidemia, said method comprising the step of administering to the subject an effective amount of an ApoA-I agonist compound according to Claim 1.

45.-53. (Canceled).

54. (Withdrawn) A method of treating a subject suffering from septic shock, said method comprising the step of administering to the subject an effective amount of an ApoA-I agonist compound according to Claim 1.

55. (Withdrawn) The method of Claim 44 or 54 in which said subject is a human.

56. (Withdrawn) The method of Claim 44 or 54 in which about 0.5 mg/kg to about 100 mg/kg ApoA-I agonist is administered to said subject.

57. (New) An ApoA-I agonist compound which is a D-enantiomeric peptide of SEQ ID NO.:4.